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### **Dietary interventions with dietitian involvement in adults with chronic kidney disease: A systematic review**

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## REVIEW - SYSTEMATIC REVIEW - META-ANALYSIS

# Dietary interventions with dietitian involvement in adults with chronic kidney disease: A systematic review

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## Abstract

**Background:** A comprehensive evidence base is needed to support recommendations for the dietetic management of adults with chronic kidney disease (CKD). The present study aimed to determine the effect of dietary interventions with dietitian involvement on nutritional status, well-being, kidney risk factors and clinical outcomes in adults with CKD.

**Methods:** Cochrane Central Register of Controlled Trials, CINAHL, MEDLINE, PsycINFO and EMBASE.com were searched from January 2000 to November 2019. Intentional weight loss and single nutrient studies were excluded. Risk of bias was assessed using the Cochrane risk-of-bias tool. Effectiveness was summarised using the mean difference between groups for each outcome per study.

**Results:** Twelve controlled trials (1906 participants) were included. High fruit and vegetable intake, as well as a multidisciplinary hospital and community care programme, slowed the decline in glomerular filtration rate in adults with stage 3–4 CKD. Interventions addressing nutrition-related barriers increased protein and energy intake in haemodialysis patients. A Mediterranean diet and a diet with high *n*-3 polyunsaturated fatty acids improved the lipid profile in kidney transplant recipients.

**Conclusions:** A limited number of studies suggest benefits as a result of dietary interventions that are delivered by dietitians and focus on diet quality. We did not identify any studies that focussed on our primary outcome of nutritional status or studies that examined the timing or frequency of the nutritional assessment. This review emphasises the need for a wider body of high-quality evidence to support recommendations on what and how dietetic interventions are delivered by dietitians for adults with CKD.

## KEYWORDS

nutrition, diet, dietitian, chronic kidney disease

## INTRODUCTION

Dietary interventions appropriate to the stage of chronic kidney disease (CKD) and treatment modality (including dialysis and kidney transplantation) are critical to the management

and progression of the condition. Recommendations have traditionally focused on nutrients considered to impact upon kidney disease progression, as well as those that accumulate as a result of a declining glomerular filtration rate. Prescriptive diets have focused on restricting intake of

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sodium, protein, potassium, phosphorus and fluid, yet targeted single and multiple nutrient restrictions in CKD have demonstrated largely inconclusive effects on CKD progression and cardiovascular events.<sup>1,2</sup> Those with CKD report that living with these dietary restrictions is overwhelming, challenging and burdensome,<sup>3,4</sup> which is reflected in poor adherence.<sup>5</sup> To support and implement best evidence-based practice, dietitians are seeking to identify, appraise and summarise contemporary evidence pertaining to the efficacy and implementation of dietary interventions delivered to people with CKD. In 2017, a Cochrane review of dietary interventions in CKD,<sup>6</sup> encompassing whole diet, dietary patterns or behaviour modification dietary interventions focusing on clinical outcomes such as mortality and cardiovascular events, concluded that dietary intervention studies were of very low quality and insufficient to guide clinical practice. This review, however, did not hone in on interventions with dietitian involvement (either in the planning or delivery stage), nor examine intervention timing or frequency. Therefore, in 2018, the British Dietetic Association Renal Nutrition Group formed a committee to investigate the evidence for the efficacy and timing and/or frequency of dietary interventions, involving dietitians, for adults with CKD. A full search and appraisal of existing guidelines<sup>1,2,7–10</sup> using the AGREE II framework was undertaken. Generally, limited evidence was found in the existing guidelines for recommendations regarding the initiation, timing, frequency and delivery of the dietetic care process in the management of CKD, and dietitian involvement was unclear (personal communication with the British Dietetic Association Renal Nutrition Group Executive, 2019). Because dietitians hold clinical expertise in the nutritional management of long-term conditions, focusing on studies with their involvement could highlight meaningful evidence.

In light of the lack of evidence in existing guidelines and the 2017 Cochrane review,<sup>6</sup> this review adopts a broader and pragmatic remit and includes evidence from randomised, quasi-randomised and non-randomised controlled trials. The objective was to review the evidence base for dietary interventions with dietetic involvement in the design or delivery, aiming to examine the impact of nutrition assessment and dietary interventions on nutritional outcomes, quality of life (QoL), patient reported experience measures (PREMs), kidney and cardiovascular disease (CVD) risk factors and clinical outcomes in adults with CKD. To enhance the clinical applicability of this review, studies must have reported implementation details including the timing or frequency of the dietary intervention.

## METHODS

### Protocol registration

The protocol for the systematic review was registered with PROSPERO (CRD42019151455).<sup>11</sup> The present study is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.<sup>12</sup>

### Literature search

We searched Cochrane Central Register of Controlled Trials (CENTRAL, via the Cochrane Library), CINAHL, MEDLINE and PsycINFO (all via Ebscohost), and EMBASE.com, from January 2000 to November 2019, for randomised controlled trials (RCTs), quasi-RCTs and non-randomised trials that were designed and/or delivered by dietitians in adults with any stage of CKD with a follow-up of at least 6 months. The search year 2000 was chosen to reflect the year that the first K/DOQI nutritional guidelines for kidney disease were published.<sup>7</sup> Studies of multi-nutrient, dietary pattern or 'whole diet' behavioural, lifestyle or nutrition counselling interventions for the purpose of improving nutritional outcomes, QoL, risk factors for kidney, or cardiovascular disease and clinical outcomes were eligible for inclusion. A detailed search strategy for EMBASE is provided in the Supporting information, Doc. S1. We checked bibliographies of original studies and recent review articles for additional relevant studies.

### Study selection

Two of the investigators (TJB and HM/HW) independently screened titles and abstracts for all identified studies and retrieved the full texts of potentially relevant studies for further screening. Full-text assessments were performed according to the *a priori* selection criteria that are detailed in the registered protocol.<sup>11</sup> Studies were included if they were: (i) full-text articles published from year 2000 onwards or accepted for publication, and written in the English language; (ii) RCTs, quasi-RCTs and non-RCTs evaluating the effect of multi-nutrient or 'whole diet' behavioural, lifestyle or nutrition counselling interventions, including nutritional assessment, with dietitian involvement in the development or delivery of the intervention; (iii) conducted in adults with CKD stage 1 to 5, including individuals with kidney failure treated with haemodialysis, peritoneal dialysis, kidney transplantation or supportive/conservative care; and (iv) had a follow-up of  $\geq 6$  months and reported details of the frequency and timing of the intervention. Any setting and any mode of delivery were included. Types of control group included any other type of intervention, no treatment and standard care. Studies focusing on weight loss or single nutrients were excluded because these have been reviewed elsewhere or are being updated.<sup>13–16</sup>

### Data extraction

Two of the investigators (TJB and HM/HW) independently extracted data on: (i) study characteristics (first author, year of publication, trial registration, country, sponsor/funding, study design, duration of intervention and follow-up, sample size and eligibility criteria); (ii) participants' characteristics

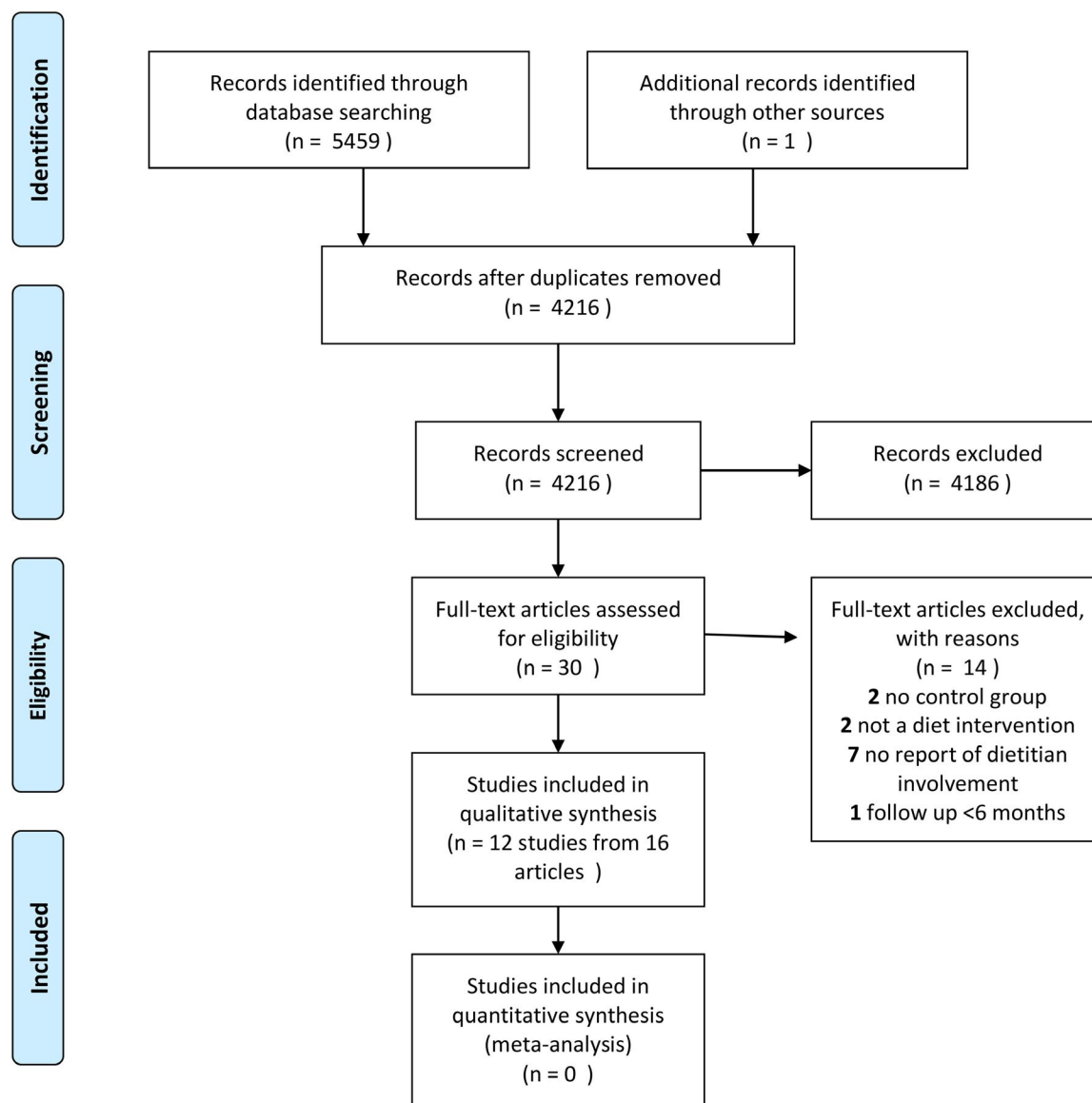


FIGURE 1 PRISMA flow diagram. Flow chart describes the process of selection of studies within the systematic review

(age, gender, and baseline estimated glomerular filtration rate [eGFR]); (iii) methods for dietary implementation and tailoring/modification reported using the Template for Intervention Description and Replication (TIDieR) checklist<sup>17</sup>; and (iv) outcome measures. Our primary outcome was nutritional status, and other outcomes included QoL, nutritional outcomes such as diet quality and anthropometry, PREMs, kidney and CVD risk factors (hyperlipidaemia, hyperglycaemia, hypertension and proteinuria) and clinical outcomes.

### Assessment of risk of bias

Two of the investigators (TJB and HW) independently assessed the risk of bias at the study level using Cochrane's risk-of-bias assessment,<sup>18</sup> with disagreements discussed with a third investigator (HM) to reach a consensus. Reviewers

were not blinded with respect to study authors, institution or journal. We assessed trials as 'high' risk for attrition bias if attrition was  $\geq 30\%$ . We searched for both trial registrations and protocols to assess selective outcome reporting. For cluster-randomised trials, we made an additional assessment regarding the timing of randomisation and recruitment to clusters.<sup>19</sup>

### Data synthesis

The outcomes were reported by CKD stage and treatment modality, sub-grouped by type of intervention. Effectiveness was summarised using the mean difference between groups in each study, at the last available follow-up, for each outcome. In studies where the mean difference between groups at follow-up was not reported, the mean change from baseline or the absolute values at baseline and follow-up for each group were reported and the

summary of effectiveness was assessed as unclear. Given the limited number of studies and variation in the types of interventions, comparisons and study populations, it was not appropriate to pool any of the data in meta-analysis or conduct further statistical analyses, including statistical evaluation of publication bias, sensitivity analysis or measurement of heterogeneity.

## RESULTS

### Study selection

Figure 1 details the flowchart of the study selection process. Our electronic search identified 5459 potentially relevant records. One additional record was identified through other sources. Of these, 1244 were excluded as duplicates and 4186 were excluded after screening for titles and abstracts. We performed full-text screening of the remaining 30 records, and 12 studies (from 16 articles – four companion papers) were included. The characteristics of the included studies, including details of the providers of the interventions and comparators, are provided in the Supporting information (Table S1). There were 10 RCTs, one quasi-RCT and one non-randomised trial with participants self-allocating to groups. Participants included people with CKD stages 3 and/or 4 ( $n = 5$  studies), haemodialysis ( $n = 3$  studies) and kidney transplantation ( $n = 4$  studies). The mean age of participants ranged from 41 to 69 years; mean percentage males within each study ranged from 26.9% to 72%. The mean eGFR ranged from 21.6 to 42.6 mL min<sup>-1</sup> 1.73 m<sup>-2</sup> for people with stages 3–4 CKD and 48.4 to 53.8 mL min<sup>-1</sup> 1.73 m<sup>-2</sup> for kidney transplant recipients.

The types of dietary interventions varied, although there were three broad models of delivery: personalised interventions; multidisciplinary team (MDT) interventions; and food-based interventions. Personalised interventions included: telehealth to support dietary self-management<sup>20,21</sup>; individualised nutrition and exercise counselling<sup>22</sup>; lifestyle advice using self-monitoring<sup>23</sup>; individualised nutrition education<sup>24</sup>; and dietary intervention tailored to patient-specific barriers.<sup>25,26</sup> MDT interventions included: cooking classes plus an exercise programme<sup>27</sup> and an integrated (hospital and community) care programme.<sup>28</sup> Food-based interventions included: diet to increase base-reducing fruit and vegetable intake to reduce dietary acid by 50%<sup>29–31</sup>; diet to increase the intake of omega-3 polyunsaturated fatty acids (PUFAs)<sup>32</sup>; and Mediterranean diet.<sup>33–35</sup> More information on each intervention, including delivery format, setting and tailoring, is provided in the TIDieR checklist in the Supporting information (Table S2). The study sample sizes ranged from 37 to 570 and the total sample was 1906 participants. The mean length of active intervention ranged from 6 months to 5 years.

### Assessment of risk of bias

Risk of bias was 'unclear' in most of the domains (Figure 2; see also the Supporting information, Doc S1). Nine of the 12

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Other bias - timing of recruitment of clusters
Flesher 2011	?	?	?	?	+	?	?	
Goraya 2013	?	?	-	?	+	?	+	
Goraya 2014	?	?	-	?	+	?	+	
Henggeler 2018	+	+	-	?	+	?	+	
Jiamjariyapon 2017	?	?	?	?	+	+	?	-
Karavetian 2015	-	?	?	?	?	-	-	-
Kelly 2019	+	+	-	?	+	+	+	
Kuningas 2019	+	+	-	?	+	+	+	
Leon 2001	?	?	-	?	?	?	?	-
Leon 2006	+	?	-	-	+	?	+	-
Sabbatini 2013	-	-	-	?	+	?	+	
Stachowska 2005	?	?	-	?	?	?	?	

FIGURE 2 Risk of bias summary. Summary describes review authors' judgements about each risk of bias item for each included study. ?, risk of bias is unclear; +, low risk of bias; -, high risk of bias

studies were rated as 'high' risk of performance bias because the participants and/or the providers were not blinded to the intervention. We rated nine studies as 'low' risk of attrition bias. Three studies were rated as 'high' risk of bias in three domains each, including two studies that did not randomly allocate participants. All four cluster RCTs were rated high risk of bias relating to the timing of recruitment of the clusters. Other issues to highlight are: (i) very few studies reported whether confounding factors such as lipid-lowering drugs, antihypertensive and steroid medications were equally balanced across groups at baseline or controlled for in analyses and (ii) none of the studies that reported on clinical outcomes were adequately powered to detect changes in such endpoints.<sup>21,23,28</sup>

### Effects of dietary intervention

Table 1 summarises effectiveness and includes outcome data from 11 of the 12 included studies. We only extracted



TABLE 1 Summary of effectiveness

Study	Nutritional status	Renal and CVD risk factors (lipids, BP, eGFR, proteinuria, albuminuria)	Diet quality	Body composition	Functional markers	Quality of life	Cardiovascular events
<i>Summary of effectiveness<sup>a</sup></i>							
CKD stages 3–4							
Flesher <i>et al.</i> (2011) <sup>27</sup>	NR	↔ BP, eGFR, lipids, proteinuria	NR	NR	NR	NR	NR
Goraya <i>et al.</i> (2013) <sup>30</sup>	NR	↑ Albuminuria, SBP vs HCO <sub>3</sub> , ↔ eGFR vs HCO <sub>3</sub>	NR	↑ vs HCO <sub>3</sub>	NR	NR	NR
Goraya <i>et al.</i> (2019) <sup>29</sup> ; Goraya <i>et al.</i> (2019) <sup>31</sup>	NR	↑ LDL, SBP vs HCO <sub>3</sub> and vs UC, ↑ eGFR vs UC, ↔ eGFR vs HCO <sub>3</sub> , ↑ albuminuria vs UC, ↔ albuminuria vs HCO <sub>3</sub> , ↔ HDL vs HCO <sub>3</sub> and vs UC	↑ F&V vs HCO <sub>3</sub> and vs UC	↑ BMI, WT vs HCO <sub>3</sub> and vs UC	NR	NR	NR
Jiamariyapon <i>et al.</i> (2017) <sup>28</sup>	NR	↑ eGFR, TG, ↔ LDL, proteinuria, ↓ SBP	NR	↔ BMI	NR	↔	↔ All-cause mortality, cardiovascular events (acute MI and stroke), ESRD, 50% increase in serum creatinine from baseline, ↑ composite clinical endpoint
Kidney transplant							
Hengeler <i>et al.</i> (2018) <sup>22</sup>	?	↔ Lipids	NR	↔	↔	↔	NR
Kuningas <i>et al.</i> (2019) <sup>23</sup>	NR	↔ Albuminuria, BP, eGFR, lipids	NR	↑ FM, WT, ↔ FFM, SFT, WHR	↔	↔	NR
Sabbatini <i>et al.</i> (2013) <sup>32</sup>	NR	↑ Albuminuria, lipids, proteinuria, ↔ eGFR	↑ n-3 PUFA, n-6:n-3 PUFA ratio, PUF&F, SF, ↔ F (% kcal), MUSF (% kcal), n-6 PUFA	↑	NR	NR	↔ No major adverse cardiac events
Stachowska <i>et al.</i> (2006) <sup>33</sup> ; Stachowska <i>et al.</i> (2005) <sup>34</sup> ; Stachowska <i>et al.</i> (2005) <sup>35</sup>	NR	↑ TC, TG, ↔ BP, HDL, ? LDL	NR	↔ BF, BMI, LM <sup>b</sup> , WHR	NR	NR	NR
Haemodialysis							
Karavetian <i>et al.</i> (2015) <sup>24</sup>	NR	NR	NR	NR	NR	NR	NR
Leon <i>et al.</i> (2001) <sup>26</sup>	NR	NR	NR	NR	NR	NR	NR
Leon <i>et al.</i> (2006) <sup>25</sup>	↔	NR	↑ protein + energy intake	↔	NR	↔	NR

Abbreviations: BF, body fat; BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; F&V, fruit and vegetables; F, fat; FFM, fat free mass; FM, fat mass; HCO<sub>3</sub>, bicarbonate; LM, lean mass; MI, myocardial infarction; MUSF, monounsaturated fat; NR, not reported; TC, total cholesterol; UC, usual care; WHR, waist hip ratio; WT, weight.

<sup>a</sup>↓, intervention not effective; ↑, intervention effective; ↔, unable to assess effectiveness; note, effectiveness is assessed using between group differences at last available time point.

<sup>b</sup>Increase in lean mass from baseline in control group.

feasibility data<sup>20</sup> and not effectiveness data<sup>21</sup> for one study because the control group received a delayed intervention, and so did not receive 6 months of the same treatment (our inclusion criteria states a minimum follow-up of 6-months). Detailed outcome results are provided in the Supporting information (Table S3).

## CKD stages 3 and 4

### *Personalised interventions*

Participants of a dietitian-led, theory-based, telehealth coaching intervention<sup>20</sup> to support dietary self-management viewed it as an acceptable alternative to face-to-face clinic consultations. The study uptake rate was 35%, with 93% of the intervention group and 98% of the control group completing the study. Intervention participants received phone calls every 2 weeks for 3 months and tailored text messages for 6 months to encourage a diet following guidelines for CKD. The control group had usual care (UC) for the initial 3 months followed by non-tailored educational text messages for months 3–6. Eighty-two percent of participants needed at least two calls to begin putting planned dietary intentions in place. All of the participants in the intervention identified the tailored text messages as useful for supporting dietary self-management, and 27 (69%) of the control group reported that the non-tailored text messages were useful for supporting change.

### *Multidisciplinary team interventions*

Group-based cooking and exercise classes in addition to standard care did not significantly improve against *a priori* defined targets for kidney and CVD risk factors (lipids, blood pressure [BP],<sup>28</sup> eGFR, proteinuria) in 40 participants at 12 months.<sup>27</sup> Process evaluation indicated an improvement in exercise frequency and concern over health condition in the intervention group and improved communication with healthcare providers in the control group. An integrated community-based care programme (in addition to standard care plus a group-based educational programme) showed inconsistent results across outcomes in 387 participants at 24 months.<sup>28</sup> There were no significant differences between groups for body mass index, low-density lipoprotein (LDL), proteinuria, QoL, all-cause mortality, cardiovascular events (acute myocardial infarction and stroke), end-stage kidney disease or 50% increase in serum creatinine from baseline. There were significant differences between groups indicating improvement for intervention participants for eGFR (adjusted mean difference 2.74; 95% confidence interval [CI] = 0.60–4.50 mL min<sup>-1</sup> 1.73 m<sup>-2</sup>), triglycerides (mean difference -18.15; 95% CI = -35.5 to -0.8 mg dL<sup>-1</sup>) and the composite clinical endpoint of acute myocardial infarction, stroke, end-stage kidney disease and a 50% increase in serum creatinine from baseline (hazard ratio = 0.59; 95% CI = 0.37–0.96). Systolic BP (SBP) was lower in the control group compared to intervention participants during follow-up (mean difference 5.37; 95% CI = 3.4–7.3).

### *Food-based interventions*

Increasing the intake of fruit and vegetables compared to sodium bicarbonate showed additional improvement in some kidney and CVD risk factors (albuminuria, SBP) and weight (mean difference -6.4 kg at 12 months;  $p < 0.01$ ) and no change in plasma potassium at 12 months (mean plasma potassium  $4.1 \pm 0.2$  mEq L<sup>-1</sup> for both groups at baseline and 12 months) (one study, 73 participants with stage 4 CKD).<sup>30</sup> The same type of intervention by the same study team showed improvement in some kidney and CVD risk factors (albuminuria, eGFR, LDL, SBP), diet quality, and body composition at 5 years (one study, 108 participants with stage 3 CKD)<sup>29,31</sup> when fruit and vegetable intake was increased compared to UC. The 5-year net eGFR decrease was significantly less with sodium bicarbonate (-12.3; 95% CI = -12.9 to -11.7 mL min<sup>-1</sup> 1.73 m<sup>-2</sup>) and fruit and vegetables (-10.0; 95% CI = -10.6 to -9.4 mL min<sup>-1</sup> 1.73 m<sup>-2</sup>) compared to UC (-18.8; 95% CI = -19.5 to -18.2 mL min<sup>-1</sup> 1.73 m<sup>-2</sup>) but was not significantly different between sodium bicarbonate and fruit and vegetable groups. The fruit and vegetable group showed additional improvement for body mass index, diet quality, LDL and SBP at 5 years compared to sodium bicarbonate (all  $p < 0.05$ ). The 5-year net change in fruit and vegetable intake in cups per day was 2.1 (2.0–2.2) for fruit and vegetables, 0.0 (-0.07 to 0.1) for sodium bicarbonate and was 0.0 (-1.0 to 0.09) for UC. LDL (mg dL<sup>-1</sup>) decreased by 45.5 (-51.0 to -40.0) with fruit and vegetables, by 21.5 (-27.0 to -16.0) with sodium bicarbonate and by 14.3 (-20.6 to -9.2) with UC. SBP decreased with fruit and vegetables by an additional 8 mmHg compared to sodium bicarbonate ( $p < 0.05$ ) and an additional 13.3 mmHg compared to UC ( $p < 0.05$ ). There was no difference between the three groups for high-density lipoprotein at 5 years.<sup>29,31</sup>

## Kidney transplantation

### *Personalised interventions*

Individualised lifestyle interventions (including diet and exercise) that used motivational interviewing<sup>22</sup> or behaviour change techniques<sup>23</sup> did not improve lipids, QoL or functional markers (two studies, 139 participants) after 6–12 months compared to UC or control. However, in one of these studies, UC involved relatively well-resourced dietetic input of between one and four consultations within 1 year.<sup>22</sup> One of these studies<sup>23</sup> also reported on BP, eGFR and albuminuria and showed no significant difference between groups; there were no serious cardiac events reported in either group. That study<sup>23</sup> reported improvements in weight (mean difference -2.47 kg; 95% CI = -4.01 to -0.92) and fat mass (mean difference -1.53 kg; 95% CI = -2.94 to -0.12) but not in skinfold thickness and fat free mass at 6 months (interim report – follow-up planned for 10 years) compared to control. The other study<sup>22</sup> measured nutritional status (patient-generated subjective global assessment) and reported that two of 19 intervention participants had 'suspected malnutrition' at baseline and another intervention

participant developed 'suspected malnutrition' at 6 months following hospitalisations.

#### *Food-based interventions*

A diet to increase the intake of omega-3 PUFAs and to decrease the omega-6:omega-3 ratio showed improvement in some kidney and CVD risk factors (lipid profile, proteinuria, albuminuria), some components of diet quality (saturated fat, polyunsaturated fat, *n*-3 PUFA, *n*-6:*n*-3 PUFA ratio) and body weight compared to standard dietetic advice in 50 participants at 6 months. There was no difference in eGFR, total fat intake, monounsaturated fat or *n*-6 PUFA.<sup>29</sup> A Mediterranean diet intervention showed improvement in some kidney and CVD risk factors (total cholesterol, triglycerides) compared to a low-fat diet in 37 participants at 6 months. There was no difference in HDL, BP or body composition (lean mass increased in controls) and inconsistent reporting of LDL across companion papers.<sup>33–35</sup>

## Haemodialysis

#### *Personalised interventions*

One study<sup>24</sup> compared three groups: individualised nutrition education by a dietitian with dedicated time (2 h month<sup>-1</sup> patient<sup>-1</sup> delivered as 2 × 15-min sessions per week), nutrition education by a hospital dietitian (around other duties) and standard care (dietitian not specifically trained for CKD management) on management of osteodystrophy (570 participants, data reported for 394 [69%] completers only). Both intervention group dietitians were trained in stage-based behaviour change and dietary management of CKD. Dietary knowledge and stages of change were assessed, although only within groups (not between groups); study contamination was also reported. Individualised nutrition education by a dietitian with dedicated time was associated with an improvement in dietary knowledge score from baseline, although improvement in behaviour stage from 'preparation' to 'action' at 6 months was not maintained at 12 months follow-up.

Two studies<sup>25,26</sup> by the same study team tailored a dietary intervention to patient-specific barriers (poor nutritional knowledge, poor appetite, help needed with shopping or cooking, low fluid intake, inadequate dialysis dose, depression, difficulty chewing, difficulty swallowing, gastrointestinal symptoms and acidosis). The pilot study<sup>26</sup> did not report on any of our pre-specified outcomes. The follow-on study<sup>25</sup> demonstrated that an intervention tailored to address patient-specific barriers increased protein and energy intake (mean difference 4.7 kcal kg<sup>-1</sup> day<sup>-1</sup> for energy and 0.2 g kg<sup>-1</sup> day<sup>-1</sup> for protein intake ( $p < 0.05$ ) at 12 months), although nutritional status, body composition or QoL did not change at 12 months compared to UC provided by nephrologists, dietitians and social workers (one study, 208 participants). At baseline, intervention participants were more likely to have low fluid intake and difficulty swallowing,

whereas control participants were more likely to have poor appetite. The most common barriers in both groups were poor nutritional knowledge and poor appetite. There were significant improvements at 12 months in favour of the intervention in terms of the percentage of participants overcoming barriers related to poor nutritional knowledge, help needed with shopping or cooking and difficulty swallowing, compared to UC.

## DISCUSSION

As far as we are aware, this is the first review of nutrition interventions, for adults with CKD, that are specifically delivered or designed by dietitians, focusing on studies of multi-nutrient, dietary pattern or 'whole diet' behavioural, lifestyle or nutrition counselling interventions, within controlled study designs. Our review complements the 2017 Cochrane review<sup>6</sup> on nutrition interventions in CKD, which assessed mortality and cardiovascular events. By contrast to the Cochrane review, our review examined a broader range of outcomes and focussed on dietary interventions provided or developed by dietitians specifically. Our review also complements the Kidney Disease Outcomes Quality Initiative (KDOQI) National Kidney Foundation 2020 guidelines for nutrition in CKD, where the authors recognise that they provide information on dietary management rather than all intervention strategies.<sup>36</sup>

The evidence is largely uncertain, with few available studies, a range of interventions and outcomes measured, and mixed results of limited strength. A limited number of studies suggest some benefits of nutrition interventions that are delivered by dietitians and focus on dietary quality. High fruit and vegetable intake and a multidisciplinary group-based programme may slow eGFR decline in stages 3–4 CKD. Furthermore, an increased intake of fruit and vegetables appeared to confer additional advantage in improving BP control, LDL cholesterol levels and weight reduction compared to the use of sodium bicarbonate and standard care. A Mediterranean diet and a diet with a high *n*-3 PUFA intake may improve blood lipids in adults who have had a kidney transplant. These study findings support the importance of diet quality and a holistic approach to diet and indicate a role for further research into this subject.

In haemodialysis, individualised interventions addressing nutrition-related barriers may increase protein and energy intake. Increases in energy and protein intake of 200–350 kcal and 6–11 g protein day<sup>-1</sup> from foods and food fortification may provide economic benefits if reducing the requirement for prescribed oral nutritional supplements. This supports the development and validation of tools for use in outpatient/ambulatory settings to identify not only nutritional risk, but also specific barriers that may impact on nutritional risk or nutritional status. Overcoming barriers requires the identification of these barriers and a multidisciplinary approach to the treatment of nutritional concerns. Many studies on the use of oral nutrition supplements in



haemodialysis were excluded from this review as a result of their duration being less than 6 months. Therefore, we were unable to evaluate the effect of supplements on nutritional status or other outcomes.

As a result of the limited number of studies, of which there was considerable variation in the type of interventions and comparators, meta-analysis was not possible. There is insufficient and poorly reported data on nutritional status, and there were no studies identified that met the inclusion criteria and examined the timing or frequency of assessment of nutritional status. Furthermore, none of the studies was primarily aimed at maintaining or improving nutritional status, which was the primary outcome of this review. Frequency of nutritional assessment to improve or maintain a well-nourished state is a key question for the dietetic workforce, and an innovative trial design may be needed to determine whether more or less frequent nutrition assessment has an impact on clinical outcomes such as malnutrition, hospitalisation, quality of life and mortality.

Innovative study design and methods of delivery may be required to deliver dietetic interventions including ongoing support for dietary change, at scale. One study by Kelly *et al.*<sup>20</sup> suggests that newer methods of delivery such as text messaging may be well received by service users and provides a way of optimising the use of limited dietetic resource. This was the only included study to report on the patient experience of the intervention. Our search identified a protocol for a study (KIDNEYTEXT),<sup>37</sup> which has subsequently published feasibility results in January 2021.<sup>38</sup> KIDNEYTEXT included three text messages per week (in addition to standard care) designed to improve dietary behaviours, and demonstrated that this type of intervention was feasible and acceptable to people on maintenance haemodialysis. Further research is required to determine whether generic and/or individualised text messaging may be effective, and provide a practical solution to improve access to dietetics services within staffing and economic constraints.

## Strengths and limitations of the review

The remit was to review the evidence for the effectiveness of dietary interventions in adults with CKD within the context of studies that reported implementation details including the timing or frequency of the dietary intervention aiming to increase clinical applicability. Studies of weight loss and single nutrient studies were excluded because they have already been reviewed or are being updated.<sup>13–16</sup> We have evaluated the evidence from studies that investigate different types of dietary modification, such as increasing PUFAs; lifestyle interventions that are underpinned by behaviour change theory, including self-monitoring and motivational interviewing; interventions using different method of delivery, such as text messaging and telephone; and interventions that investigate different practices, including integrated care (hospital and community) and dietitian care with dedicated time. As well as extracting information on how each study

was implemented, using the TIDieR principles, we have extracted process indicators such as participation, retention, fidelity and satisfaction. There is insufficient evidence to make recommendations on what and how dietetic interventions are delivered. The lack of available evidence may reflect inherent difficulties in conducting controlled trials in dietetics. We have already highlighted the variation in comparators and the complexity of evaluating multicomponent interventions. Other inherent difficulties include the necessary assumption that patient populations are relatively homogenous, although the main principle of a dietetic intervention is its individualised nature based on a complex assessment including physical, anthropometric, psychological and socio-economic factors. An innovative pragmatic trial design is needed to capture the assessment and identified need process, aiming to measure effectiveness.

Despite a comprehensive and wide search of the literature, widening the search to include non-randomised trials as well as RCTs, the evidence identified was limited. There were no identified studies of dietary interventions in adults undergoing peritoneal dialysis, in supportive care or with CKD stages 1 and 2, and so it was not possible to assess the effectiveness of such interventions in the early stages of CKD or with these specific treatment modalities. We can be confident that we have identified all the controlled intervention evidence available reporting on the timing and/or frequency of dietetic interventions, excluding single nutrient and weight loss interventions, for adults with CKD, which was designed or provided by dietitians, with a duration of at least 6 months follow-up. It is possible that we missed some published studies with dietitian involvement because it was not reported in the abstract; however, in an attempt to mitigate this, we obtained the full-text article for further assessment, if it appeared in the abstract that the intervention was multidisciplinary and it met our other inclusion criteria.

Risk of bias was generally 'unclear', with a high risk of performance bias as a result of a lack of blinding of participants in nine studies. There were other important issues with the quality of the evidence that impact on the certainty of the evidence: very few studies reported whether confounding factors such as lipid-lowering and antihypertensive medications were equally balanced across groups at baseline or controlled for in subsequent analyses; none of the studies were adequately powered to detect changes in clinical endpoints.

Broadly, there was inconsistency both within and across studies in terms of whether an intervention showed improvement or no difference compared to the control; where there was no difference between groups, both groups had improved from baseline. In general, most studies were small, and may have been underpowered to detect differences in outcomes, particularly as a result of heterogeneity in the studied populations, an inadequate length of follow-up for clinical events and myriad factors influencing changes to behaviour beyond the control of researchers in these studies. Standard care control groups varied considerably across the

studies. Standard care usually involved some dietetic input, ranging from UC from a hospital dietitian to individualised dietary counselling and regular review by a renal (kidney) dietitian. In four studies,<sup>20,27,30,31</sup> the provider of the control was not reported; in two studies,<sup>23,28</sup> there was no dietetic input in the control group, and six studies<sup>22,24–26,32,34</sup> clearly state that a dietitian provided care in the control group. In one of these studies, control participants received up to four consultations with a renal (kidney) dietitian during 12 months following kidney transplant.<sup>22</sup> Therefore, many of these studies assessed enhanced dietetic input rather than dietetic input *per se*. This might at least partially explain the lack of effect for interventions and standard care may reflect an adequate level of care with some interventions. In addition, many of the included studies were multicomponent interventions (e.g., interventions including diet and physical activity) and so it is difficult to identify any potential effects of the dietary component alone, within these studies.

## CONCLUSIONS

The evidence is largely uncertain. A limited number of studies suggest some benefits of dietary interventions that are delivered by dietitians and focus on diet quality or whole diet interventions. There is currently insufficient evidence to draw any conclusions for dietetic practice, specifically regarding the initiation, timing and frequency of the delivery of dietary interventions, as well as the implementation of such by dietitians. This review highlights the need for more high-quality evidence to support recommendations on what and how dietetic interventions are delivered and measured by dietitians for adults with CKD.

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## CONFLICT OF INTERESTS

The authors have no conflicts of interest.

## AUTHOR CONTRIBUTIONS

HM, HW and TB developed the review protocol. TB conducted the research. HM, HW and TB analysed the data and wrote the paper. All authors contributed to the interpretation of the data. HM had primary responsibility for final content. All authors read and approved the final manuscript submitted for publication. Authors declare human ethics approval was not needed for this study.

## TRANSPARENCY DECLARATION

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with PRISMA guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned (PROSPERO registration number CRD42019151455) have been explained.

## PEER REVIEW

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## AUTHOR BIOGRAPHIES



**Tamara J. Brown** has held Research Fellow posts in 7 UK universities and conducted over 20 systematic reviews and written over 50 peer-reviewed journal articles and scientific reports for national and international funders. She is particularly interested in interventions for behavioural risk factors for non-communicable disease, such as lifestyle interventions for obesity

prevention. She is passionate about translating evidence-based research into practice and enjoys helping practitioners to deliver the best care, through undertaking systematic reviews, from protocol development through to publication and dissemination.





**Harriet Williams** is a Dietitian with 14 years of experience in working with people with kidney disease. Harriet graduated from the University of Surrey with a BSc (Hons) in Human Nutrition and Dietetics in 2006 before returning home to Anglesey where she now leads the wider Dietetic service as Head of Dietetics for the West area of Betsi Cadwaladr University

Health Board. Harriet is passionate about the positive impact good dietetic care can have for people with a variety of disease conditions and believes firmly that the central role of the Dietitian is to support people to achieving a better quality of life, through their health and enabling them to enjoy their diet.



**Bruno Mafrici** is the current Chair of the Renal Nutrition Group of the British Dietetic Association UK and he is an associate lecturer at the University of Nottingham and Birmingham City University. He has an interest in delivering advanced dietetic practice in patients with kidney disease and currently works at Nottingham University Hospitals NHS Trusts.



**Helena S. Jackson** has been a renal dietitian for over 20 years. She has a particular interest in nutrition screening and the role of diet in the prevention and management of kidney disease. She has contributed to the article as a member of the British Dietetic Association Renal Nutrition Group Guideline Working Party.



**Lina Johansson** is interested in furthering the evidence base to improve the health and wellbeing of people with kidney disease through nutrition. Her recent work has focused on investigating nutrition parameters/ education in people with: non-dialysis kidney disease, transplant and on dialysis. This article is a product of a collaboration with a working group from the specialist

British Dietetic Association group (Renal Nutrition Group) formed to understand the evidence base behind research in CKD involving the dietitian/nutritionist.



**Fiona Willingham** has over 20 years clinical experience working as a specialist renal dietitian. Her main clinical and research interests are nutritional care in pre-dialysis, nutritional screening and assessment, and exercise and nutritional interventions to improve health and quality of life outcomes in patients approaching and commencing dialysis. She is actively involved with the British Dietetic Association Renal Nutrition Group Committee.



**Ashleigh McIntosh** is a recent dietetic graduate hoping to complete a PhD in the future. She is interested in researching all aspects of diet and disease and understanding the impact of dietetic interventions on chronic diseases. Her research during her masters has focused on the impact of food and eating behavioural problems on the outcomes of bariatric therapy and diet

quality indices and their associations with health-related outcomes in children and adolescents.



**Helen L. MacLaughlin** focuses her work on nutritional interventions to improve health in those with kidney disease. This work was a collaborative effort led by the British Dietetic Association Renal Nutrition Group.

## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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